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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,500	12/05/2005	Takashi Suzuki	OKA-0230	1582

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1633	

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04/30/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,500	SUZUKI ET AL.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-24* is/are pending in the application.

4a) Of the above claim(s) *19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-18, 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 1/24/2010 was entered.

Amended claims 11-22 and new claims 23-24 are pending in the present application.

Applicants elected previously cultured mammalian cell derived from gonad as the elected species without traverse.

Claim 19 was withdrawn from further consideration because it is directed to a non-elected species.

Amended claims 11-18, 20-22 and new claims 23-24 are examined on the merits herein with the above elected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-14, 16, 18, 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. ***This is a new ground of rejection necessitated by Applicant's amendment.***

Claims 11-14,16, 18, 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is a thawing step of the rapidly frozen cultured mammalian cell; and without this essential thawing step a

cultured mammalian cell extract liquid would not be obtained and used in subsequent steps for a cell-free protein synthesis method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11, 15-18, 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chatterjee et al. (US 200/20168706) in view of Wagner et al (US 6,630,358). ***This is a new ground of rejection necessitated by Applicant's amendment.***

Chatterjee et al disclose an in vitro peptide/protein synthesis comprising mixing RNA templates with at least cell extracts, and incubating the mixtures under conditions

sufficient to produce one or more peptides or proteins encoded by all or a portion of the templates (see at least Summary of the Invention, particularly paragraphs 43-45 and 62-63), wherein **cell extracts are derived from prokaryotic or eukaryotic or insect cells or cell lines (paragraphs 78-79, 100), including mammalian cells such as NIH3T3, CHO, COS, C127, VERO, BHK, HeLa, 293** and that cell extracts can be prepared by any method used in the art that maintains the integrity of the transcription/translation system or if the process damages one or more component necessary for any stage of transcription/translation, the damaged component can be replaced or substituted for after the extraction preparation (paragraphs 100, 102). Chatterjee et al also teach that an exemplified incubation mixture contains at least Hepes/KOH at pH8.2, K-glutamate, $Mg(OAc)_2$, DTT, ATP, GTP, UTP, CTP, each of the amino acids (paragraphs 104-105) and the reactions were carried out at 37^0C (paragraphs 128, 135).

Chatterjee et al do not teach specifically the step of rapidly freezing a cultured mammalian cell suspended in an extraction solution in 10 seconds of less in the preparation of a cultured mammalian cell extract.

At the effective filing date of the present application, Wagner et al already disclosed a preparation of a mammalian cell lysate by suspending cultured human cells in **ice-cold hypotonic buffer** containing DNase/RNase and **a mixture of protease inhibitors**, allowing the cells to swell in a microcentrifuge tube for 5 minutes, **lysing the cells by rapidly freezing in liquid nitrogen and thawing in ice-cold water**; the cell debris and precipitates were removed by high-speed centrifugation and the supernatant is cleared by passage through a 0.45 um filter (see col. 32, line 65 continues to line 8 of

col. 33). It is noted that the instant specification teaches simply that a cell suspension was rapidly frozen in liquid nitrogen for the preparation of cultured mammalian cell extract liquid (see example 2) and defines the term "rapid freezing" to be meant that a cultured mammalian cell is frozen in not longer than 10 sec, preferably not longer than 2 sec (page 8, lines 4-6). Therefore, the step of lysing mammalian cells in a microcentrifuge tube by rapidly freezing in liquid nitrogen by Wagner et al would also result in freezing the cells in 10 seconds or less. Additionally, ice-cold water should have a temperature within the temperature range of -10 ^{0}C to 20 ^{0}C recited in claim 17.

It would have been obvious for an ordinary skilled artisan to modify the method taught by Chatterjee et al by also preparing a cultured mammalian cell extract by lysing cultured mammalian cells in a microcentrifuge tube by rapidly freezing in liquid nitrogen and thawing in ice-cold water as taught by Wagner et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because Wagner et al already taught successfully a preparation of a mammalian cell lysate by suspending cultured human cells in **ice-cold hypotonic buffer** containing DNase/RNase and **a mixture of protease inhibitors**, allowing the cells to swell in a microcentrifuge tube for 5 minutes, **lysing the cells by rapidly freezing in liquid nitrogen and thawing in ice-cold water**; the cell debris and precipitates were removed by high-speed centrifugation and the supernatant is cleared by passage through a 0.45 um filter. Furthermore, Chatterjee et al teach clearly that cell extracts can be prepared by any method used in the art that maintains the integrity of the transcription/translation system or if the process damages one or more component

necessary for any stage of transcription/translation, the damaged component can be replaced or substituted for after the extraction preparation.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Chatterjee et al., Wagner et al., coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chatterjee et al. (US 200/20168706) in view of Wagner et al (US 6,630,358) as applied to claims 11, 15-18, 20-21 above, and further in view of Reiter et al. (US 6,475,725; Cited previously).

The combined teachings of Chatterjee et al and Wagner et al were already presented above. However, none of the references teaches specifically the use of CHO derived from CHO K1-SFM. It is also noted that the instant application provides no limiting definition of a CHO K1-SFM cell. Therefore, the limitation is construed based on its plain meaning in the art as a CHO K1 cell adapted for growth in serum free medium.

At the effective filing date of the present application, Reiter et al already disclosed production of recombinant proteins in CHO cells adapted for growth in serum- and protein-free medium (see throughout, especially col. 6, line 31 through col. 7, line 15) and taught that CHO-K1 cells as a preferred cell type for preparing recombinant proteins (col. 6, line 49).

Accordingly, it would have been obvious for an ordinary skilled artisan in the art to further modify the combined teachings of Chatterjee et al and Wagner et al by also using the CHO-K1-SFM cell of Reiter et al for preparation of a cell extract to be used in the *in vitro* peptide/protein synthesis system of Chatterjee et al and Wagner et al. In *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), the Supreme Court particularly emphasized "the need for caution in granting a patent based on a combination of elements found in the prior art," (*Id.* At 1395) and discussed circumstances in which a patent might be determined to be obvious. Importantly, the Supreme Court reaffirmed principles based on it precedent that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results."(*Id.* At 1395.).

In the instant case, the combined method of Chatterjee et al and Wagner et al differs from the method presently claimed only in the substitution of CHO cell for the CHO K1-SFM required by the instant claim. However, the teachings of Reiter et al demonstrate that CHO K1-SFM cells and their use in the expression of recombinant proteins were known in the art at the time of the present invention was made. An ordinary skill in the art could have selected CHO K1-SFM of Reiter et al for preparation of a cell extract to be used in the *in vitro* peptide/protein synthesis system of Chatterjee et al and Wagner et al. with a predictable outcome, particularly Chatterjee et al teach explicitly that cell extracts can be derived from any prokaryotic or eukaryotic cells or cell lines.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chatterjee et al. (US 200/20168706) in view of Wagner et al (US 6,630,358) as applied to claims 11, 15-18, 20-21 above, and further in view of Gebauer et al (WO 00/50586; Cited previously).

The combined teachings of Chatterjee et al and Wagner et al were already presented above. However, none of the references teaches specifically that the solution for extraction comprises at least a potassium salt, a magnesium salt, dithiotheitol and a buffer.

At the effective filing date of the present application, Gebauer et al already taught at least that **an ice-cold hypotonic extraction buffer** containing Hepes, KOAc, Mg(OAc)2, DTT, and optionally protease inhibitors can be used for the preparation of cell-free extracts from various sources, including mammalian cells and insect cells, to be utilized in a cell-free translation system (see at least page 2, lines 23-28; page 5, lines 9-17 and example 4).

Accordingly, it would have been obvious for an ordinary skilled artisan to further modify the combined method taught by Chatterjee et al and Wagner et al. by also utilizing an ice-cold hypotonic extraction buffer containing Hepes, KOAc, Mg(OAc)2, DTT, and optionally protease inhibitors in the preparation of cell-free extracts to be utilized in a cell-free translation system in light of the teachings of Gebauer et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because Gebauer et al already taught successfully at least the use of an ice-cold hypotonic extraction buffer containing Hepes, KOAc, Mg(OAc)2, DTT for the preparation of cell-free extracts from various sources, including mammalian cells and insect cells, to be utilized in a cell-free translation system.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Chatterjee et al., Wagner et al. and Gebauer et al., coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chatterjee et al. (US 200/20168706) in view of Wagner et al (US 6,630,358) as applied to claims 11, 15-18, 20-21 above, and further in view of Choi et al (US 2002/0106719).

The combined teachings of Chatterjee et al and Wagner et al were already presented above. However, none of the references teaches specifically that the reaction liquid for cell-free protein synthesis comprising the specific components recited in claim 23.

At the effective filing date of the present application, Choi et al already taught at least a cell-free protein synthesis system comprising incubating a reaction mixture containing a cell extract (rabbit reticulocyte lysate (RRL) or CHO cell extract), creatine phosphate, creatine phosphokinase, amino acids, RNA, ATP, GTP, potassium acetate,

magnesium acetate, Hepes/KOH (pH 7.3), ribonuclease inhibitor, DTT, calf liver total tRNA mixture for 60 min at 30 ^{0}C (see at least paragraphs 30 and 53).

Accordingly, it would have been obvious for an ordinary skilled artisan to further modify the combined method taught by Chatterjee et al and Wagner et al. by also utilizing the same key components taught by Choi et al for cell free protein synthesis.

An ordinary skilled artisan would have been motivated to carry out the above modification because Choi et al already taught successfully at least a cell-free protein synthesis system comprising incubating a reaction mixture containing a cell extract (rabbit reticulocyte lysate (RRL) or CHO cell extract), creatine phosphate, creatine phosphokinase, amino acids, RNA, ATP, GTP, potassium acetate, magnesium acetate, Hepes/KOH (pH 7.3), ribonuclease inhibitor, DTT, calf liver total tRNA mixture for 60 min at 30 ^{0}C.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Chatterjee et al., Wagner et al. and Choi et al., coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 12-13 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chatterjee et al. (US 200/20168706) in view of Wagner et al (US 6,630,358) as applied to claims 11, 15-18, 20-21 above, and further in view of Inoue et al (US 2002/0123101) and Choi et al (US 2002/0106719).

The combined teachings of Chatterjee et al and Wagner et al were already presented above. However, none of the references teaches specifically of incubation of a reaction liquid for cell-free protein synthesis containing components other than an exogenous mRNA (preferably carried out at 0 ^{0}C to 50 ^{0}C, including the range of 15 ^{0}C - 37 ^{0}C) **prior to adding an exogenous mRNA**; and/or the reaction liquid or mixture comprising the specific components recited in claim 24.

At the effective filing date of the present application, **Inoue et al already taught at least that translation reaction mixtures were incubated at 37 ^{0}C for 5 minutes prior the template DNA or RNA was added to carry out the translation reaction at 37 ^{0}C** (see at least example 14, particularly paragraph 268).

Additionally, Choi et al already taught using a reaction mixture containing a cell extract (e.g., rabbit reticulocyte lysate (RRL) or CHO cell extract), creatine phosphate, creatine phosphokinase, amino acids, ATP, GTP, potassium acetate, magnesium acetate, Hepes/KOH (pH 7.3), ribonuclease inhibitor, DTT and calf liver total tRNA mixture for cell-free protein synthesis (see at least paragraphs 30 and 53).

Accordingly, it would have been obvious for an ordinary skilled artisan to further modify the combined method taught by Chatterjee et al and Wagner et al. by also incubating a translation reaction mixture without the exogenous mRNA template at 37 ^{0}C for 5 minutes prior to the start of the protein translation reaction by adding the template RNA as taught by Inoue et al; and/or utilizing the same key translation reaction components taught by Choi et al for cell free protein synthesis.

An ordinary skilled artisan would have been motivated to carry out the above modifications because Inoue et al already taught that translation reaction mixtures could be preincubated at 37 ^{0}C for 5 minutes prior to the addition of template RNA to start the translation reaction; and Choi et al already taught the use of a reaction mixture containing a cell extract (e.g., rabbit reticulocyte lysate (RRL) or CHO cell extract), creatine phosphate, creatine phosphokinase, amino acids, ATP, GTP, potassium acetate, magnesium acetate, Hepes/KOH (pH 7.3), ribonuclease inhibitor, DTT and calf liver total tRNA mixture for cell-free protein synthesis.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Chatterjee et al., Wagner et al., Inoue et al, and Choi et al., coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/QUANG NGUYEN/
Primary Examiner, Art Unit 1633